

## Secretory Activity of Human Cyst Fluid Isolated From Polycystic Kidney Disease Patients

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Polycystic kidney disease (PKD) is characterized by the slow growth of fluid-filled cysts in kidney tubules. Kidney function is relatively normal in the first 5 decades of life despite substantial cyst development but thereafter the decline in function is precipitous leading to complete renal failure in five years in 50% of patients. As cysts increase in size, the probability of rupture and release of cyst fluid becomes increasingly likely. Cyst fluid has been shown to cause an additional secretory  $\text{Cl}^-$  flux that leads to the expansion of the remaining intact cysts. We have previously shown that the active component of the cyst fluid is lysophosphatidic acid (LPA). Electrophysiological techniques were used to measure human cyst fluid stimulation of ion flux in the mpkCCD<sub>cl4</sub> cell line, a model of the cell type that lines renal cysts. The  $\text{Cl}^-$  secretory response is due to activation of both CFTR and a calcium activated chloride channel. Interestingly, the cyst fluid effect was not accompanied by an increase in cAMP but rather via a LPA receptor mediated activation of phospholipase C followed by the stimulation of the tyrosine kinase Pyk. These results suggest novel targets for treatment of late stage PKD.

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